THYROID PROFILE IN CHRONIC KIDNEY DISEASE

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CERTIFICATE

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I solemnly declare that this dissertation entitled ***"THYROID PROFILE IN CHRONIC KIDNEY DISEASE"*** was done by me at Madras Medical College and Govt. General Hospital, during 2004-2007 under the guidance and supervision of **Prof.C.Rajendiran, M.D**. This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in General Medicine (Branch - I).

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CONTENTS

ABBREVIATIONS

CKD	-	Chronic Kidney Disease
DIT	-	Diiodotyrosine
FT4	-	Free Thyroxine
GFR	-	Glomerular Filtration Rate
MIT	-	Monoiodotyrosine
T3	-	Triiodothyronine
T4	-	Thyroxine
TRH	-	Thyrotropin Releasing Hormone
TSH	-	Thyroid Stimulating Hormone
TBG	-	Thyroxine Binding Globulin

Introduction

INTRODUCTION

Chronic Kidney Disease (CKD) is a clinical syndrome due to irreversible renal dysfunction leading to excretory, metabolic and synthetic failure resulting in accumulation of nitrogenous waste products and presents with varied clinical manifestations.

End stage renal disease (ESRD) represents a clinical state in which there has been an irreversible loss of endogenous renal function, of a degree sufficient to render the patient permanently dependent upon renal replacement therapy in order to avoid life threatening uremia.

Inspite of varied etiologies, chronic kidney disease is the final common pathway of irreversible destruction of nephrons, ultimately resulting in "alteration of milieu interior" that affects every system in the body. One such system is thyroid hormonal system. Kidney is closely related to thyroid in the fact that it is the only other organ that competes for iodide clearance.[Ref. 25]

Patients with CKD have many symptoms and signs suggestive of thyroid dysfunction. These findings include dry skin, edema, sallow complexion, cold intolerance, low temperature, decreased basal

metabolic rate, lethargy, fatigue and hyporeflexia. So in CKD patients, it is difficult to exclude the diagnosis of hypothroidism on clinical grounds.[Ref. 31]

Various studies of thyroid functions in uremic patients have been carried out which have shown conflicting results. Hyperthyroidism. hypothyroidism and euthryoid state have all been reported by various studies. [Ref. 1,19,24,26,29,30,32,38,41,47,48] Prevalence of hypothyroidism in end stage renal disease has been estimated to range between 0 and 9.5 per cent.[Ref.22,31] There is also increased prevalence of goitre in these patients. The incidence of goitre has also been variously reported in literature.[Ref. 28,34,40,41,48]

In view of the variability of thyroid function tests in patients with CKD in previous studies, it was decided to undertake a prospective clinical and biochemical study of thyroid functions on CKD patients in the Institute of Internal Medicine, Madras Medical College and Government General Hospital, Chennai.

Aims and Objectives

AIMS AND OBJECTIVES

1. To study the prevalence of thyroid dysfunction in CKD.

2. To find out the types of thyroid dysfunction in CKD.

3. To determine the correlation between the thyroid dysfunction and severity of renal disease.

4. To identify the correlation between thyroid dysfunction and the severity of anemia in CKD.

5. To differentiate primary thyroid disease from thyroid dysfunction due to chronic kidney disease.

Review of the Literature

REVIEW OF THE LITERATURE

PHYSIOLOGY OF THYROID HORMONES

Thyroxine (T4) and Triiodothyronine (T3) are the principle hormones produced by thyroid gland.

Initially iodine is absorbed in the gut and is converted to iodide and transported in the blood. It is then actively transferred into the thyroid cell by *"Iodide trapping"*. The trapped iodide is *oxidized* to iodine and combines with tyrosine to form Mono iodotyrosine (MIT) and Diiodotyrosine (DIT). MIT and DIT are coupled to form T3 whereas two DIT couple to form T4. Oxidation, Iodination and coupling reactions are catalyzed by *"Thyroid Peroxidase"*. Thyroid hormones thus produced are bound with thyroglobulin until secreted.

Once secreted in the blood, it is transported in two forms. One is bound form in which T3 and T4 are bound to plasma proteins namely thyroid binding globulin, pre albumin and albumin. T4 is predominantly bound to thyroid binding globulin whereas T3 is predominantly bound to albumin. The other form is free T3 and T4. These free forms are in equilibrium with bound form.

In the periphery one third of T4 is converted to T3 by *5′ Deiodinase* and 45% to rT3 by *5 deiodinase*. They are further metabolised to Diiodothyronine. Only about 13% of T3 is produced from thyroid gland and remaining 87% is formed from T4.

TABLE - A : VARIATIONS IN THYROID HORMONES AND BINDING PROTEINS IN HYPER AND HYPOTHYROIDISM

Condition	Concentrations of binding proteins	Total Plasma T4, T3, rT3	Free Plasma T4, T3, rT3	Plasma TSH	Clinical Status
Hyperthyroidism	Normal	High	High	Low	Hyperthyroid
Hypothyroidism	Normal	Low	Low	High	Hypothyroid

CONTROL OF THYROID HORMONES

The thyroid stimulating hormone (TSH) controls the secretion of T3 and T4. It is secreted in a pulsatile manner with peak secretion at night. Its secretion is stimulated by thyrotropin releasing homrone (TRH). Both TRH and TSH release are under negative feedback of free T3 and T4.

HYPOTHYROIDISM

Hypothyroidism is a clinical syndrome caused by decreased levels of thyroid hormones. It can be *primary* in which there is intrinsic disorder of thyroid gland or it may be *secondary* in which there is pituitary or hypothalamic defect.

Florid hypothyroidism can be diagnosed clinically. The *symptoms* of hypothyroidism in descending order of frequency are:

- Tiredness, weakness
- Dry skin
- Feeling cold
- Hair loss
- Difficulty in concentrating and poor memory
- Constipation
- Weight gain with poor appetite
- Dyspnea
- Hoarse voice

- Menorrhagia (Later amenorrhea)
- Paraesthesia
- Impaired hearing

The *signs* of hypothyroidism in descending order of frequency are as follows:

- Dry coarse skin
- Cool peripheral extremities
- Puffy face, hands and feet (myxedema)
- Diffuse alopecia
- Bradycardia
- Peripheral edema
- Delayed tendon reflex relaxation
- Carpal tunnel syndrome
- Serous cavity effusions.

In biochemical studies, TSH is the single most important parameter for screening hypothyroidism. A normal TSH level rules out primary hypothyroidism but not secondary. To diagnose primary hypothyroidism TSH level should be above 20 µIU/ml or at least above 10µIU/ml if clinical features strongly suggest.

In the presence of elevated TSH, low T4 especially free T4 is necessary to confirm hypothyroidism. Circulatory free T3 is usually reduced. But it may be normal in 25% of hypothyroid patients. So T3 measurements are not reliable indicators of hypothyroidism.

HYPERTHYROIDISM

Hyperthyroidism is a clinical syndrome which results from excessive circulating levels of free thyroid hormones.

The *symptoms* of hyperthyroidism in descending order of frequency are as follows:

- Hyperactivity, irritability, dysphoria.
- Heat intolerance and sweating
- Palpitations

- ♦ Fatigue and weakness
- ♦ Weight loss with increased appetite
- ♦ Diarrhea
- ♦ Polyuria
- ♦ Oligomenorrhea, loss of libido

The *signs* of hyperthyroidism in descending order of frequency are follows:

- ! Tachycardia; Atrial fibrillation in the elderly
- ! Tremors
- ! Goitre
- ! Warm, moist skin
- ! Muscle weakness, proximal myopathy
- ! Lid retraction or lid lag
- ! Gynaecomastia

Laboratory investigations show TSH levels below normal. Free and total thyroid hormone levels are increased.

In 2 to 5% of patients, only T3 is increased and T4 is normal. This condition is called *"T3 thyrotoxicosis"*. Occasionally total and free T4 will be increased with normal T3 level. This condition is called *"T4 thyrotoxicosis"*.

NON THYROIDAL ILLNESS[Ref. 6,8,20,37,43,46]

Alteration in serum thyroid hormones occurs in wide variety of illness which predominantly affect the T3 level and no intrinsic disease of thyroid gland is detected. It is variously termed as *Low T3 syndrome, Sick euthryoid syndrome, Non thyroidal illness syndrome and Thyroid hormone adaptation syndrome*.

This syndrome occurs in wide variety of illness as follows:

i. Acute critical illness and febrile illness such as infections, myocardial infarction etc.

ii. Injuries such as burns, trauma, etc.

iii. Surgery

iv. Fasting

v. Diabetes mellitus

vi. Liver disease

vii. Renal disease

viii. Ketogenic diet

ix. Drugs such as glucocorticoids, dopamine, phenytoin and beta blockers

x. Malignancy

xi. Psychiatric illness

In non thyroidal illness state, initially there is decrease in serum T3 level, both total and free T3 (FT3). This is associated with increase in reverse T3 (rT3).

As illness progresses, there is decrease in serum T4 also, a state called *"Low T3, T4 syndrome"*. Although total T4 level decreases, the free T4 (FT4) remains normal or slightly reduced. Inspite of this reduced T3 and T4 level, serum TSH level remains normal or reduced, by which it is differentiated from primary hypothyroidism. But many studies have showed slight elevation of TSH level in Non thyroidal illness in the absence of hypothyroidism.[Ref. 7,21,26]

CHRONIC KIDNEY DISEASE

Pathophysiology

The unique property of the kidney is that in the presence of CKD, compensatory and adaptive mechanisms maintain acceptable health until the GFR is around 10 to 15 ml/min and life sustaining renal excretory and homeostatic functions continue until the GFR is above 5 ml/min.

Intact Nephron Hypothesis

The explanation proposed for these adaptive mechanism is that, in CKD there is progressive loss of nephrons, so most of the nephrons are non functioning. The remaining few functioning nephrons tend to hyper function and take an increased work load so that the overall loss of function is minimized. This indicates that GFR of the individual functioning nephrons have increased above normal, a state know as *hyperfiltration*. This increase in single nephron GFR in the functioning nephrons produce an increased volume of filtrate and their tubules respond appropriately by excreting fluids and solutes in amounts which maintain external balance. This is due to close integration of glomerulus and tubular function called "glomerulo tubular balance", which is present until the terminal stages of CKD. These above stated popular

explanations for continuing function in the remaining nephrons, is referred to as the *"intact nephron hypothesis"*.

Trade Off Hypothesis

It is described that the adaptation arising in CKD may control one abnormality, but only in such a way so as to produce other changes characteristic of uremic syndrome. The mechanism involved is unknown. This trade off hypothesis is described in hormones like parathormone, vasopressin, atrial natriuretic peptide and solutes like iodide, potassium, phosphate and others.

Uraemic Syndrome

Uraemic syndrome is a consequence of combination of the effects of the retention of waste products in all organ system and the failure of endocrine and homeostatic functions of the kidney.

These patients manifest with symptoms like fatigue, dyspnoea, facial puffiness, ankle swelling, anemia, vomiting, pruritus, polyuria, nocturia etc.

The potential toxic substances that accumulate include purine metabolites, amines, indoles, phenols, myoinositol and acid polyols.

"Middle molecules" are nitrogenous substances of molecular weight between 50 and 5000 Da. They are suspected to contribute to uraemia.

CHRONIC KIDNEY DISEASE PRESENTING AS NON THYROIDAL ILLNESS

Chronic kidney disease is one among the several conditions causing "Low T3 syndrome".

Chronic kidney disease has been divided into five stages based on the endogenous creatinine clearance. A typical patient with chronic progressive renal disease may be considered to pass through all five stages.

Stage - I

Presence of objective kidney damage with increased GFR. GFR is more than 90 ml/min.

Stage - II

Presence of kidney damage with mild decrease in GFR. GFR is 60-89 ml/min.

Stage - III

Moderate decrease in GFR. GFR is 30 - 59 ml/min with or without objective evidence of kidney damage.

Stage - IV

Severe reduction in GFR 15-29 ml/min.

Stage - V

GFR less than 15 ml/min.

As with other low T3 syndrome, CKD produces decrease in T3 when GFR falls below 50%. As the GFR decreases the reduction in T3 is more marked than T4. In ESRD, on an average, diminished T4 is found in 29% of the patients and diminished T3 in 55% of the patients.[(Ref. 31)]

TABLE - B : CHANGES IN SERUM THYROID HORMONES AND TSH CONCENTRATION IN PATIENTS WITH NON THYROIDAL ILLNESS

Conditions	Serum T3	Serum rT3	Serum T4	Serum Free T4	Serum TSH
Fasting	↓	↑	=	=	↓
Mild Illness	↓	↑	=	=, ↑	=
Critical Illness	↓	↑	↓	=, ↓	↓
Surgery, Trauma, Burns	↓	↑	↓	↓	=, ↓
Chronic Kidney Disease	↓	=	=, ↓	=, ↓	=,↓
Hepatitis	=, ↑	=, ↑	=, ↑	=, ↓	=
HIV infection	=	↓	=	=, ↓	=, ↑
Depression	=, ↓	=, ↑	=, ↑	=, ↑	=, ↓

= No Change, ↓ Decreased, ↑ Increased

The low T3 syndrome in CKD differs from other conditions causing similar illness by two unique features.[Ref. 37]

i. rT3 is usually low or normal in CKD due to redistribution into the extra vascular compartment. Some unknown factor in uremia stimulates the uptake of rT3 into the liver. [Ref.16]

ii. Increased incidence of goiter is present in CKD, Probably due to decreased clearance of iodine by the kidney.

PATHOPHYSIOLOGY OF LOW T3 SYNDROME

As stated above in CKD there is initial decrease in total T3, later T4 inspite of normal or low TSH. Various mechanisms have been proposed for the changes in thyroid profile.

According to the postulates, CKD affects thyroid homeostasis at all levels as follows:

a. Changes in Hypothalamic - Pituitary - thyroid axis

i. Sensitivity of TSH Secretion to low thyroid hormones is decreased.[Ref. 7,12,36,37,46]

ii. Limited TSH reserve.[Ref.37]

iii. Decrease in nocturnal pulses of TSH secretions is either due to changes in thyrotrophs or due to deceased TRH secretion.[Ref. 3,13,46]

iv. Tissue concentration of the hormone may be appropriate for the patient, so the patient is in euthyroid state.[Ref. 37]

v. Serum FT3 and FT4 appears normal by sensitive methods.[Ref.2,15]

b. Changes in Hormone Transport

i. Presence of protein and non protein inhibitors prevent the binding of thyroxin with thyroxin binding protein. Non protein inhibitor is non esterified unsaturated fatty acid.[Ref.18,46]

ii. Acquired intrinsic structural alteration in the T4 binding site.[Ref.20]

iii. Decrease in the concentration of thyroxine binding globulin.[Ref.37,46]

c. Changes in Metabolism

i. Decrease in the activity of Iodothyronine - 5 - Deiodinase leading to low T3.[Ref.37,46]

ii. Increase in Non-deiodinative pathways of iodothronine degradation leading to increase serum T3 sulphate, diiodothyronine, triiodo thyroacetic acid and tetra iodothryoacetic acid.[Ref. 37,46]

iii. As stated previously, there is no increase in rT3 in CKD due to increased uptake of rT3 by liver.[Ref.16,37,46]

d. Change in Plasma Membrance Transport

T3 and T4 may enter cells not only by diffusion but also by active energy dependent transport across plasma membrane.

Accumulation of the following substances prevent uptake and subsequent deiodination.[Ref.46]

(i) 3-Carboxy 4-methyl 5- propyl 2- Furane (CMPF)

(ii) Indoxyl sulphate

In uraemia the activity of thyroid hormones at nuclear level are not compromised. A Recent study showed increased receptor expression to preserve tissue euthyroidism.(Ref.45)

DIAGNOSIS OF PRIMARY THYROID DISEASES IN CKD

Recent studies have shown that the prevalence of hypothyroidism is increased in chronic kidney disease. Several clinical features of both hypothyroidism and CKD are similar. So differentiating both the conditions on clinical background is less likely. Hence all the CKD patients with symptomatology of hypothyroidism should be screened for hypothyroidism.

Hypothyroidism should be diagnosed only if the following prevails.

a. Basal TSH level should be elevated more than 20 µIU/ml.

b. Both total and free T4 are distinctly low in the presence of normal TBG.(Ref.31)

c. Presence of antithyroid antibodies provide a clue for hypothyroidism.(Ref.31)

d. rT3 is not useful because it is decreased in CKD.

Primary hyperthyroidism is very rare in CKD. This condition is diagnosed by

a. Low serum TSH

b. High serum total and free T4 concentration

High serum T4 with low T3 in the presence of CKD should raise the suspicion of T4 thyrotoxicosis. This is because serum T3 level will be suppressed in low T3 syndrome with serum T4 unaffected.[Ref.46]

MANAGEMENT

Several studies have been conducted in patients with low T3 syndrome in order to correct the thyroid profile by treating with L-thyroxine[Ref.14] and triiodothyronine.[Ref.5]

Gregory Brent et al., conducted a study in non thyroidal illness patients by treating all the patients with serum total T4 less than 5 mIU/l with 1.5. µg/kg of L-thyroxine for 2 weeks. Thyroxine level increased significantly in treated patients. Serum T3 levels was also raised. But mortality was increased in treatment groups on days 5-17.

Carter et al., studied effects of Triiodothyronine administration in patients with CKD. Study showed serum T3 level did not change over a period of 12 weeks. But the mean serum T4 and TSH levels were affected significantly. There was no subjective improvement in these patients.

Based on this observation it has been suggested that low serum T3 level in patients with severe renal failure is metabolically protective and it is interpreted as physiological adaptation to reduced basal metabolic rate and to conserve energy in an adverse environment. Hence this condition has been renamed as *"Thyroid hormone adaptation syndrome"*(Ref.46)

Administration of T4 or T3 causes suppression of TSH and increases the catabolism. So administration of thyroid hormone is not beneficial. Study also showed increased mortality with the treatment. Therefore thyroid hormones should not be given in CKD unless true hypothyroidism is documented.

PROGNOSIS

Magnitude of the thyroid dysfunction that occurs in patients with chronic kidney disease, in general, reflects the severity of the illness.

The prognosis is poor in patients with lower serum T3, T4 or TSH concentration. Studies have shown that after renal transplantation the low T3, T4 and TSH returns to normal level.[Ref.48)]

Materials and Methods

MATERIALS AND METHODS

SETTING

The study was conducted in the inpatients admitted in the Institute of Internal Medicine, Madras Medical College and Government General Hospital, Chennai.

STUDY DESIGN

Single Center

Non Randomized prospective study

STUDY PERIOD

Study was conducted between September 2005 and August 2006 for a period of 12 months.

SAMPLE SIZE

In the study period of 12 months among the patients admitted in internal medicine wards after applying inclusion and exclusion criteria 75 patients were included in this study.

The patients who fulfilled the criteria for CKD and who were on conservative management were taken into the study.

Criteria for chronic kidney disease:

1. Presence of objective kidney damage for at least three months. Kidney damage being defined as pathologic abnormalities or markers of damage including abnormalities in blood or urine tests or imaging studies. Imaging study is usually an ultra sonogram abdomen showing.

a. Bilateral contracted kidneys, or;

b. Poor corticomedullary differentiation or;

c. Type II or type III Renal parenchymal changes or;

2. Glomerular filtration rate (GFR) less than 60ml/min/1.73m^2 for at least three months with or without kidney damage.

INCLUSION CRITERIA

CKD patients who were on conservative management.

EXCLUSION CRITERIA

i. Patients with Acute Renal failure (ARF)

ii. CKD patients who underwent peritoneal dialysis or hemodialysis.

iii. CKD due to diabetes mellitus

iv. Patients with documented hypothyroidism

v. Patients on beta blockers, amiodarone, steroids, dopamine, phenytoin and iodine therapy.

vi. Other conditions like

Acute illness

Recent surgery, Trauma and Burns.

Detailed clinical history was taken from all the patients who were included in the study. History focused on symptoms of hypothyroidism like fatigue, weakness, dry skin, cold intolerance, constipation, weight gain, hoarse voice, menstrual disturbances. Past history of hypertension,

diabetes mellitus, any drug intake, history of recent surgery, trauma, jaundice and other systemic illness was taken.

After taking detailed history, all the patients were examined clinically in detail. Their height and weight was measured. A detailed General Examination was done including Nourishment, pallor, facial puffiness, pedal edema and skin texture. Presence of thyroid swelling (Giotre) was noted.

Vital signs like pulse, blood pressure, temperature were taken. All the systems were examined carefully including fundus oculi and deep tendon reflex to find out the delayed relaxation of Ankle jerk.

The following investigations were performed:

i. Blood hemoglobin level to find out the degree of Anemia.

ii. Peripheral smear study to look for pallor and the presence of burr cells.

iii. Urine examination for the presence of albumin and pus cells.

iv. Blood sugar was estimated to find out the presence of diabetes mellitus.

v. Renal parameters like serum urea and creatinine were done. From serum creatiatine value using Cockcroft - Gault formula, creatinine clearance was calculated.

vi. Serum levels of calcium and phosphorous were estimated.

vii. Chest X ray and electrocardiogram to look for features of hypothyroidism and renal failure like pericardial effusion, pleural effusion etc.

viii. Ultransonogram abdomen for features of chronic kidney disease.

ix. Serum cholesterol levels for hypothyroidism.

x. Liver function tests especially serum albumin level to find out any hypoalbuminemia in the patients.

After selecting the patients fulfilling the above criteria for the study, about 5 ml of blood sample was collected in a non heparinised sterile bottle and sent for thyroid profile.

Components of thyroid profile in this study:

- Serum Triiodothryonine (T3)
- Serum Thyroxine (T4)
- Serum Thyroid Stimulating Hormone (TSH)

Quantitative determination of the serum T3, T4 and TSH was done by Radio Immuno Assay / Immuno Radio Metric Assay.

The Normal values are

- T3 - 0.7 to 2.0 ng/ml
- T4 - 5.5 to 13.5 µg/dl
- TSH - 0.17 to 4.05 µIU/ml

Results and Observations

RESULTS AND OBSERVATIONS

Among the 75 patients included in our study 60 patentees were men accounting for 80% of the total cases. The remaining 15 patients were (20%) women.

According to the age, patients of less than 30 years were 11 in number (14.67%). Majority of the patients were in the age group between 30 and 60. 52 patients (69.33% of study population) were in this group. 12 patients (16.0%) were above the age of 60.

The creatinine clearance in this study was ranging from 7 ml/min to 38 ml/min. Patients were grouped into four groups for the purpose of further analysis based on creatinine clearance. Patients with GFR of 10 and below were 14 in number. GFR of 11 to 20 were 38 patients. GFR between 21 and 30 were 11 patients and 12 patients had GFR more than 30.

Blood urea in our study ranged from 65 of 185 mg/dl. Creatinine was in the range of 2.2 to 14.7 mg/dl.

Ultrasound abdomen showed evidence of CKD in all the 75 patients. Bilaterally contracted kidneys were present is 65 (86.7%)

patients. Remaining 10 patients (13.3%) had poor Cortico medullary differentiation.

Among the 75 patients, low serum T3 level was found in 40 patients (53.3%). Eight patients among the low serum T3 level also had high TSH value of more than 20 µIU/ml with low T4 level and also symptoms suggestive of hypothyroidism. These patients as per the criteria were grouped under *"Primary hypothyroidism"*.

14 patients had slightly elevated TSH ranging between 5 and 20 µIU/ml. Eight patients had TSH in the range of 10 to 20 µIU/ml. In the eight patients only five patients had low T4 level, among which only one patient had few clinical features of hypothyroidism. So these patients did not satisfy the criteria for hypothyroidism. So all the remaining 32 patients were grouped under *"Low T3 Syndrome"*.

TABLE - 1 SERUM CONCENTRATION OF THYROID PROFILE

Thyroid Profile	Normal Range	Study Range	Mean	Std. Deviation	Mean Excluding Hypothyrodism	Std. Deviation
Serum T3 ng/ml	0.7-2.0	0.2.-2.0	0.68	0.45	0.72	0.46
Serum T4µg/dl	5.5-13.5	0.8-9.2	5.70	2.22	6.12	1.94
Serum TSH µIU/ml	0.17-4.05	0.5-28.5	5.91	7.80	3.54	3.77

TABLE - 2 : DISTRIBUTION OF THYROID PROFILE IN OUR STUDY

Thyroid Status	No. of Patients	Percent
Hypothyroidism	8	10.67
Low T3 Syndrome	32	42.67
No Thyroid Dysfunction	35	46.67

TABLE - 3 DISTRIBUTION OF THYROID DYSFUNCTION IN THE STUDY

Thyroid Dysfunction	No. of Patients	Percent
Low T3 Syndrome	32	42.67
Low T4 Syndrome	16	21.33
Hypothyroidism	8	10.67

HYPOTHYROIDISM IN CKD

Symptoms of hypothyroidism like tiredness, somnolence, weight gain, cold intolerance, constipation, hoarse voice etc were studied in CKD. In our study population, 45 patients (60%) had the symptoms of

hypothyroidism (Table - 4). Among the 45 patents, all the eight hypothyroid patients had the symptoms.16(50%) of the 32 low T3 syndromes patients had hypothyroid symptoms. In CKD without thyroid dysfunction, 21patients (60%) had the symptoms.

TABLE - 4 ANALYSIS OF HYPOTHYOID SYMPTOMS IN CKD

Variants	No. of Patients with Hypothyroid Symptoms	Percent
Low T3 Syndrome (n=32)	16	50
Hypothyroidism (n=8)	8	100
CKD without thyroid dysfunction (n=35)	21	60

Sinus bradycardia was present in nine patients of which three patients were hypothyroid both clinically and biochemically. Delayed ankle jerk was present in 11 patients of which only 2 patients were hypothyroid.

Hypothyroidism did not show any linear correlation with GFR. Maximum number of hypothyroid patients of four in number were present in GFR 11-20 ml/min group whereas two patients each were found to be hypothyroid in the GFR less than 10 and 21-30 ml/min

group. No patients were hypothyroid in GFR greater than 30 ml/min group.

In our study diffuse thyroid swelling was present in 3 patients. Two of these patients had normal serum T3 and T4. One patient had low serum T3 and T4 with normal serum TSH.

Age comparison of low T3 syndrome patients in table 5 shows about 40.0% of CKD patients below 30 years of age have low T3 syndrome. The percentage increases to 52.2% in the age group 31-60 years. This is probably due to high number of CKD patients who are in this age group. In the age above 60 years 36.4% have low T3 Syndrome.

TABLE - 5 : AGE INCIDENCE OF LOW T3 SYNDROME EXCLUDING HYPOTHYROIDISM

Age (in years)	Number of Patients	Low T3 Syndrome	Percent
≤ 30	10	4	40.0
31-60	46	24	52.2
> 60	11	4	36.4

P Value 0.556
(Not significant)

TABLE - 6 : SEX INCIDENCE OF LOW T3 SYNDROME EXCLUDING HYPOTHYROIDISM

Sex	Number of Patients	Low T3 Syndrome	Percent
Male	54 (80.6%)	25	46.3
Female	13 (19.4%)	7	53.8

P Value 0.624

(Not significant)

Sex incidence in this study (Table - 6) show that 46.3% of males have low T3 syndrome and 53.8% of females have low T3 syndrome after excluding hypothyroid patients in the analysis.

TABLE - 7 : RESULTS OF SERUM T3, T4 AND TSH EXCLUDING HYPOTHYROIDISM

Thyroid Profile	No of Pts. with below normal value	%	No of pts. with normal value	%	No of Pts. with above normal value	%
T3	32	47.76	35	52.24	-	0
T4	16	23.88	51	76.12	-	0
TSH	-	0	53	79.10	14	20.90

TABLE - 8 DISTRIBUTION OF SERUM T3 AND T4

Creatinine Clearance ml/min	Serum T3				Serum T4			
	Normal T3		Low T3 Syndrome		Normal T4		Low T4 Syndrome	
	No of Pts.	%	No of Pts.	%	No of Pts.	%	No of Pts.	%
≤ 10	3	25	9	75	8	66.7	4	33.3
11-20	16	47.1	18	52.9	25	73.5	9	26.5
21-30	6	66.7	3	33.3	6	66.7	3	33.3
> 30	10	83.3	2	16.7	12	100	0	0
Statistical Significance	* P.0.025				P Value 0.177 Not significant			

Note * denote significant at 5% level

Observation of T3 in the Study

T3 level in this study varied from 0.2 to 2.0 ng/ml. The mean value of T3 is 0.68 ng/ml (Table - 1). Excluding the patients with primary hypothyroidism, the mean value was 0.72 ng/ml. This value is within the low normal limit. The patients with low serum T3 (low T3 syndrome) were analysed with creatinine clearance. In patients with creatinine clearance above 30 ml/min were having low T3 syndrome only in 16.7%. This rises to 33.3% and 52.9% in creatinine clearance 21-30, 11-20 groups respectively. (Table - 8). Patients with less than 10

ml/min creatinine clearance had 75% incidence of low T3 syndrome. This progressive increase in the incidence of low T3 syndrome as the renal failure progresses is statistically significant at 5% level with a P value of 0.025.

Excluding hypothyroidism, serum T3 levels were studied in relation to creatinine clearance (Table - 9). The mean value progressively decreases as the renal failure progresses with statistical significance in Tukev - HSD test at 1% level, the P value being 0.002.

None of the patients had serum T3 levels above the normal.

TABLE - 9 CORRELATION OF THYROID PROFILE WITH SEVERITY OF RENAL FAILURE EXCLUDING HYPOTHYROIDISM

Creatinine Clearance ml/min	**Mean T3 ng/ml**	**Std. Deviation**	**Mean T4 µg/dl**	**Std. Deviation**	**Mean TSH µIU/ml**	**Std. Deviation**
≤ 10 (n=12)	0.45	0.28	5.33	2.27	3.98	4.42
11-20 (n=34)	0.64	0.40	6.02	1.99	3.26	3.76
21-30 (n=9)	0.92	0.45	5.86	1.72	3.41	3.81
> 30 (n=12)	1.05	0.53	7.38	0.97	3.97	3.50
Statistical Significance	** P Value 0.002		P Value 0.061 Not Significant		P Value 0.921 Not significant	

Note ** denotes significant at 1% level.
(Significant with Tukev - HSD test)

Observation of T4 in the Study

Serum T4 level in the study varies from 0.8 to 9.2 µg/dl. Mean value of serum T4 among the 75 patients is 5.70 µg/dl. Excluding hypothroid patients the mean value is 6.12 µg/dl. This value is within low normal level of T4.

Excluding 8 hypothyroidism patients who have low T4 values, 16 (21.33%) other patients had T4 level below normal and low T3 syndrome.

Number of patients with low T4 does not correlate with severity of renal disease (Table 8). The mean value of T4 excluding hypothyroidism patients was normal at all the stages of renal failure (Table - 9) except, when the creatinine clearance was below 10 mg/ml where it was below normal. The mean serum T4 was not significant with severity of renal disease, P value being 0.061.

None of the patients had T4 value above normal level.

Observation of TSH in the Study

The value of TSH varied from 0.5 to 28.5 µIU/ml with the mean of 5.91 µIU/ml. Excluding hypothyroidism the mean TSH value is 3.54 µIU/ml. This is in normal range.

In spite of low serum T3 level in 40 (53.33%) patients, serum TSH is normal in 53. (70.67%) patients and valued between 4-20 µIU/ml is present is 14 (18.67%) patients. It is elevated more than 20 µIU/ml in 8 (10.67%) patients.

In our study the mean value of serum TSH is within normal limits in all groups of progressive renal disease (Table - 9). The values of TSH did not show any linear correlation with creatinine clearance.

TABLE - 10 DISTRIBUTION OF SERUM T3 AND T4 WITH HEMOGLOBIN LEVELS

Hemoglobin g/dl	Serum T3				Serum T4			
	Normal T3		Low T3		Normal T4		Low T4	
	No of Pts.	%	No of Pts.	%	No of Pts.	%	No of Pts.	%
≤ 6	1	16.7	5	83.3	3	50.0	3	50.0
6.1-8	7	33.3	14	66.7	14	66.7	7	33.3
8.1-11	22	68.8	10	31.3	28	87.5	4	12.5
> 11	5	62.5	3	37.5	6	75.0	2	25.0
Statistical Significance	* P.0.019				P Value 0.113 Not significant			

Note * denote significant at 5% level

Hemoglobin Level and its Correlation with Thyroid Profile in the Study

Anaemia was almost universal in our study in chronic kidney disease. Among the 75 patients, 65 of the patients had hemoglobin values less than 11g/dl. Patients hemoglobin values correlated with the severity of renal disease.

On analysing patients with low T3 levels with Hemoglobin values, as the hemoglobin level decreases, the percentage of patients having low T3 increases. (Table - 10). This is significant with P value of 0.019. When compared with low serum T4, hemoglobin values are not significantly related.

When correlating mean serum T3 and T4 with severity of anemia (Table - 11), as the hemoglobin declines, the mean T3 values also decreases. Serum mean T3 is 0.94 in the hemoglobin more than 11 group. It is 0.84, 0.54, 0.37 ng/ml in hemoglobin 8.1 - 11, 6.1-8, < 6 g/dl groups respectively. This is significant with P value of 0.010.

Mean serum T4 also has a linear correlation with hemoglobin level. The mean value of T4 is 6.35 µg/dl in hemoglobin more than 11 g/dl patients. It is 6.82 µg/dl in the hemoglobin 8.1 - 11 g/dl group,

which may be because of the increased number of patients in this group. The mean T4 decreases linearly with decreased level of hemoglobin. It is 5.44 µg/ml and 4.48 µg/dl corresponding to hemoglobin 6.1-8 g/dl and <6 g/dl respectively. This relationship is statistically significant with P value of 0.009.

TABLE - 11 CORRELATION OF THYROID PROFILE WITH SEVERITY OF ANAEMIA EXCLUDING HYPOTHYROIDISM

Hemoglobin g/dl	Serum T3		Serum T4	
	Mean	Std. Deviation	Mean	Std. Deviation
< 6	0.37	0.23	4.48	2.63
6.1 - 8	0.54	0.30	5.44	1.79
8.1 - 11	0.84	0.48	6.82	1.60
> 11	0.94	0.56	6.35	2.03
P value	0.010**		0.009**	

Note ** significant at 1% level.

Figure - 1
Distribution of Thyroid Profile in the Study

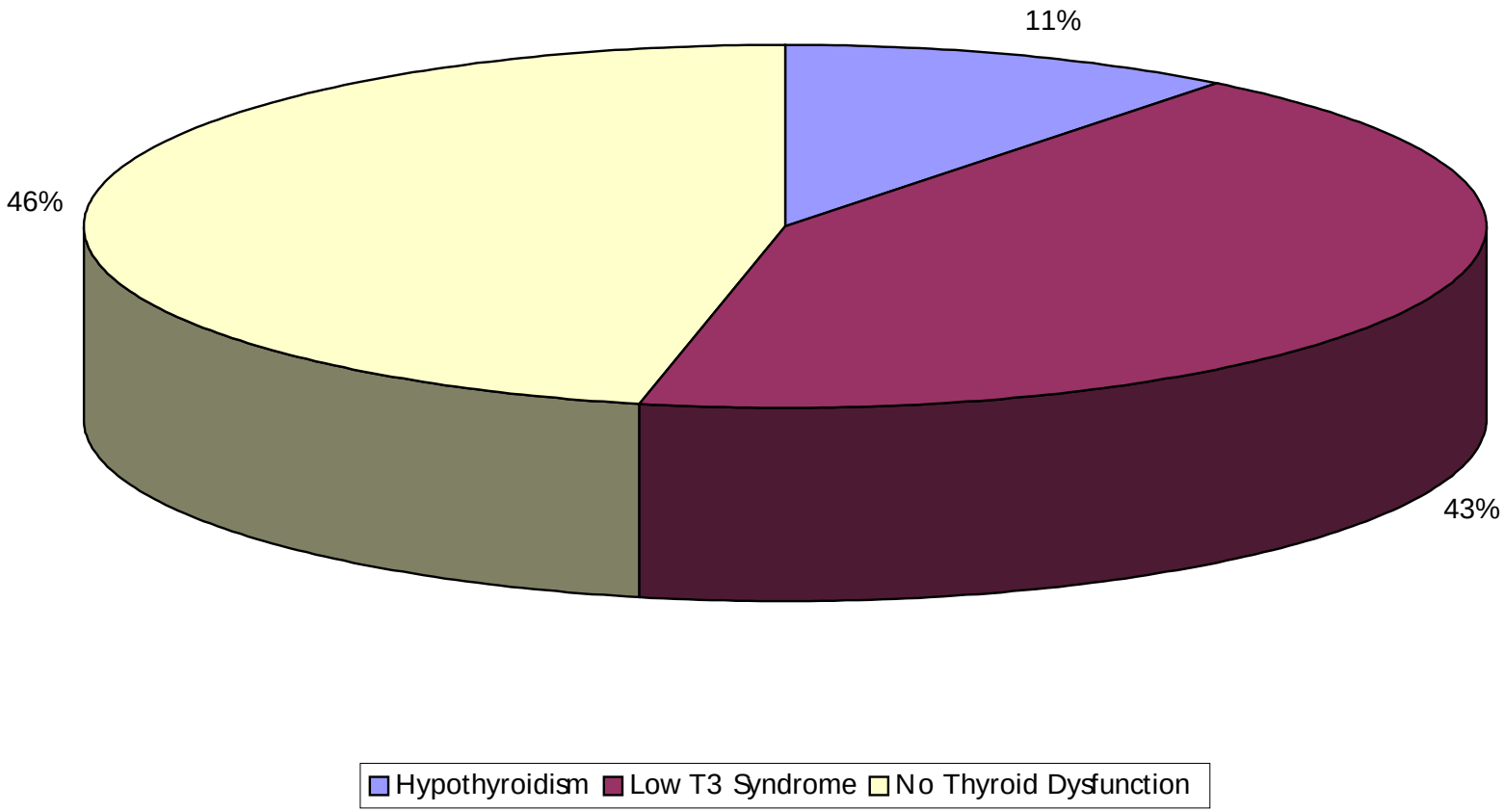


Figure- 2
Analysis of Hypothyroid Symptoms in CKD

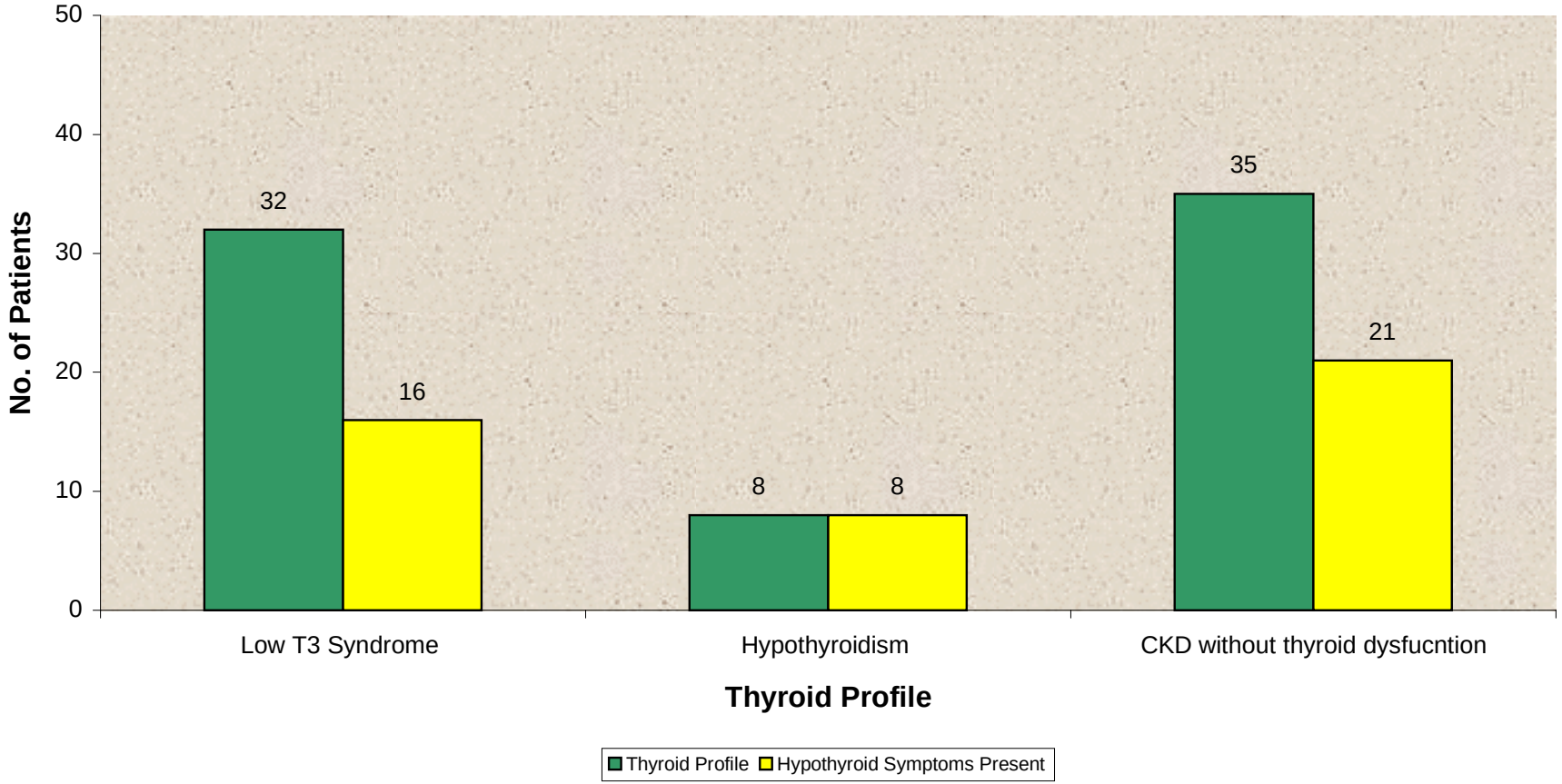


Figure - 3

Age Incidence of Low T3 Syndrome Excluding Hypothyroidism

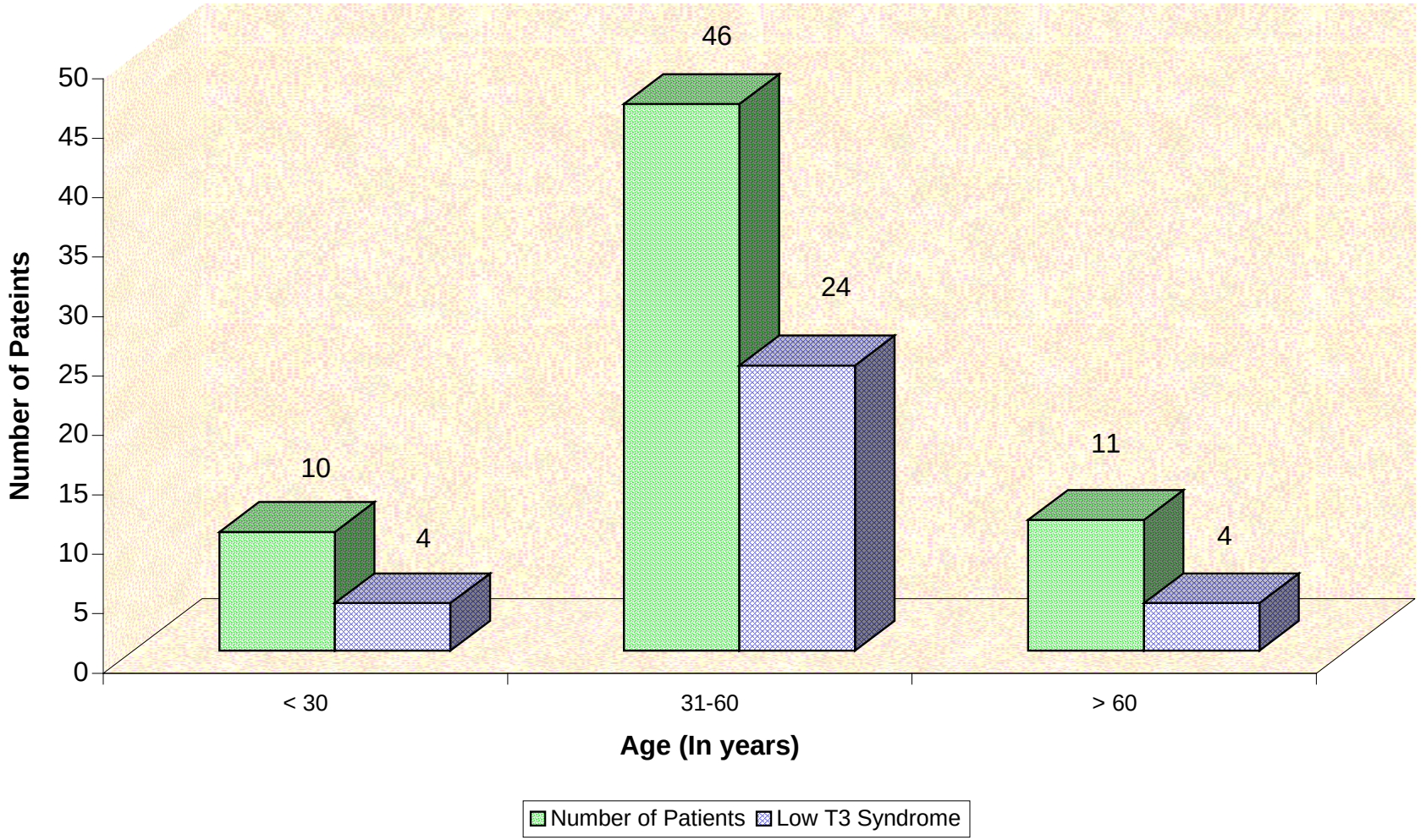


Figure - 4

Sex Incidence of Low T3 Syndrome Excluding Hypothyroidism

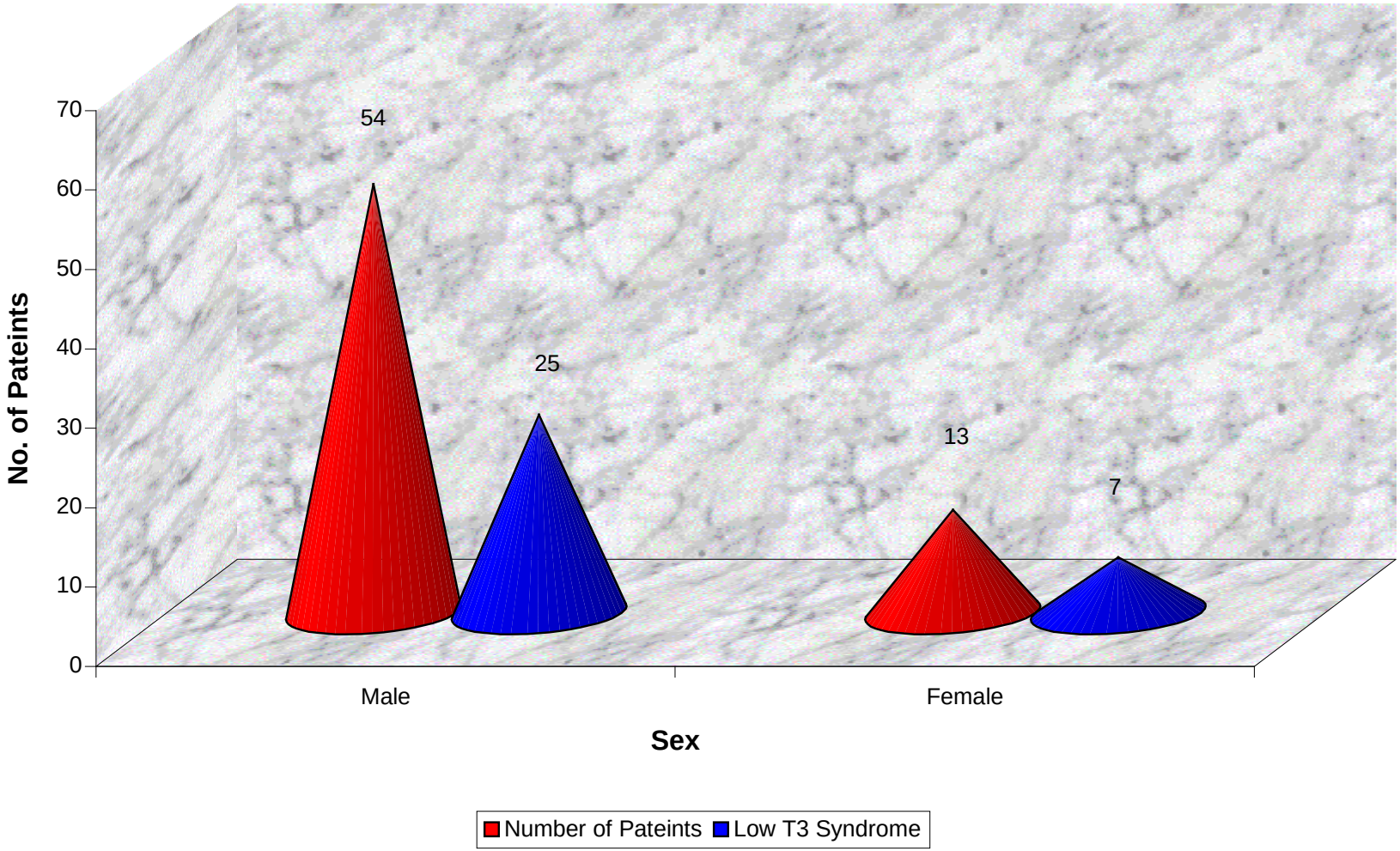


Figure - 5
Results of Serum T3 Excluding Hypothyroidism

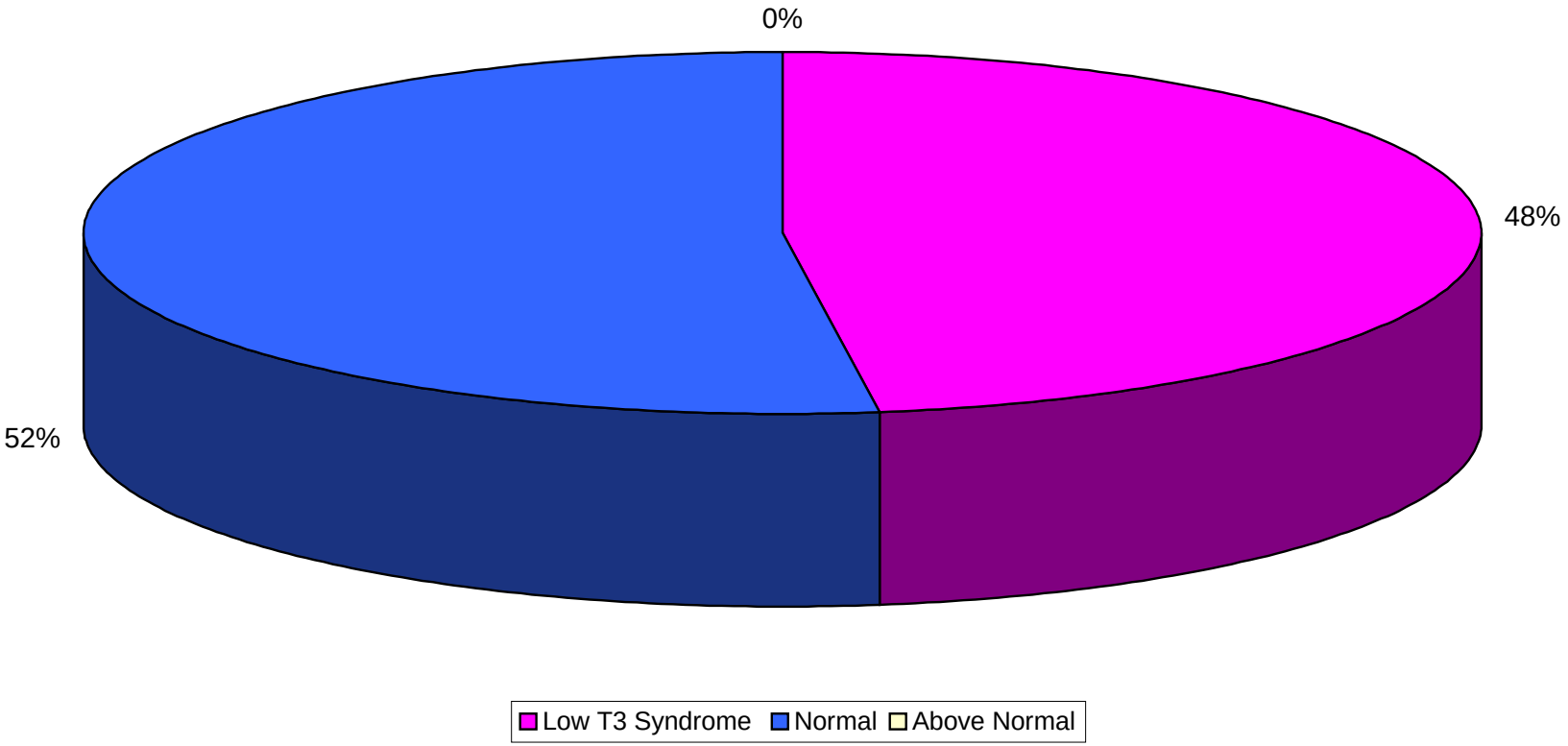


Figure - 6
Resuts of Serum T4 Excluding Hypothyroidism

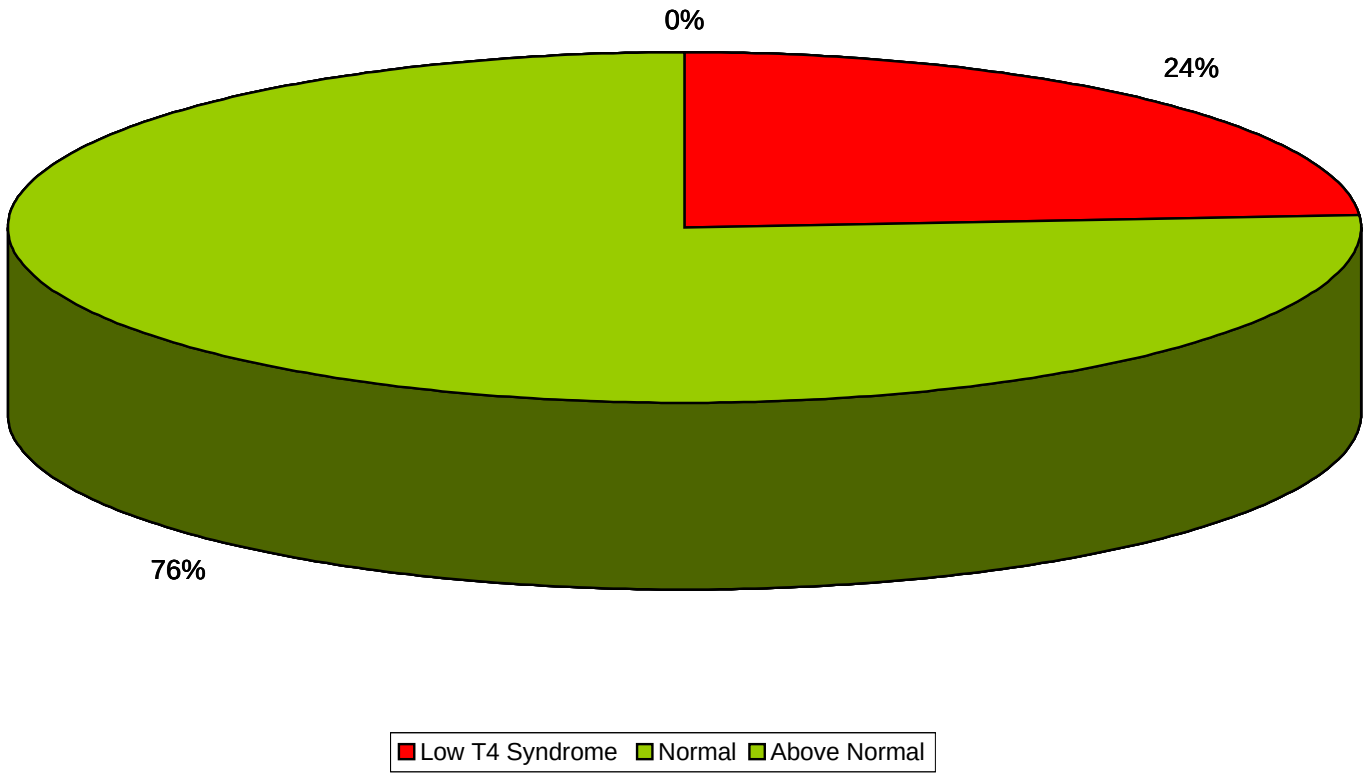


Figure - 7
Distribution of Serum T3 and T4 with Creatinine Clearance

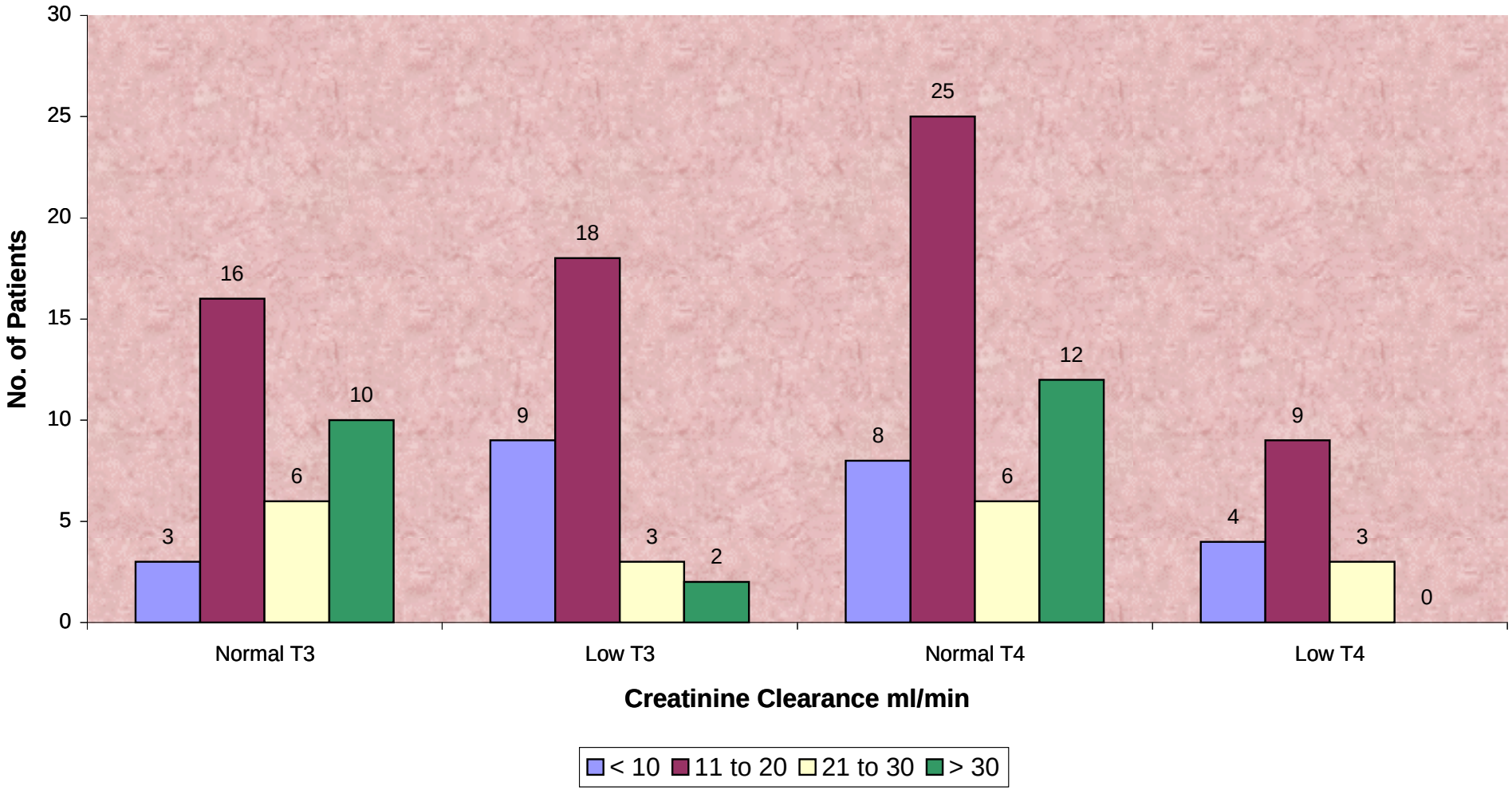
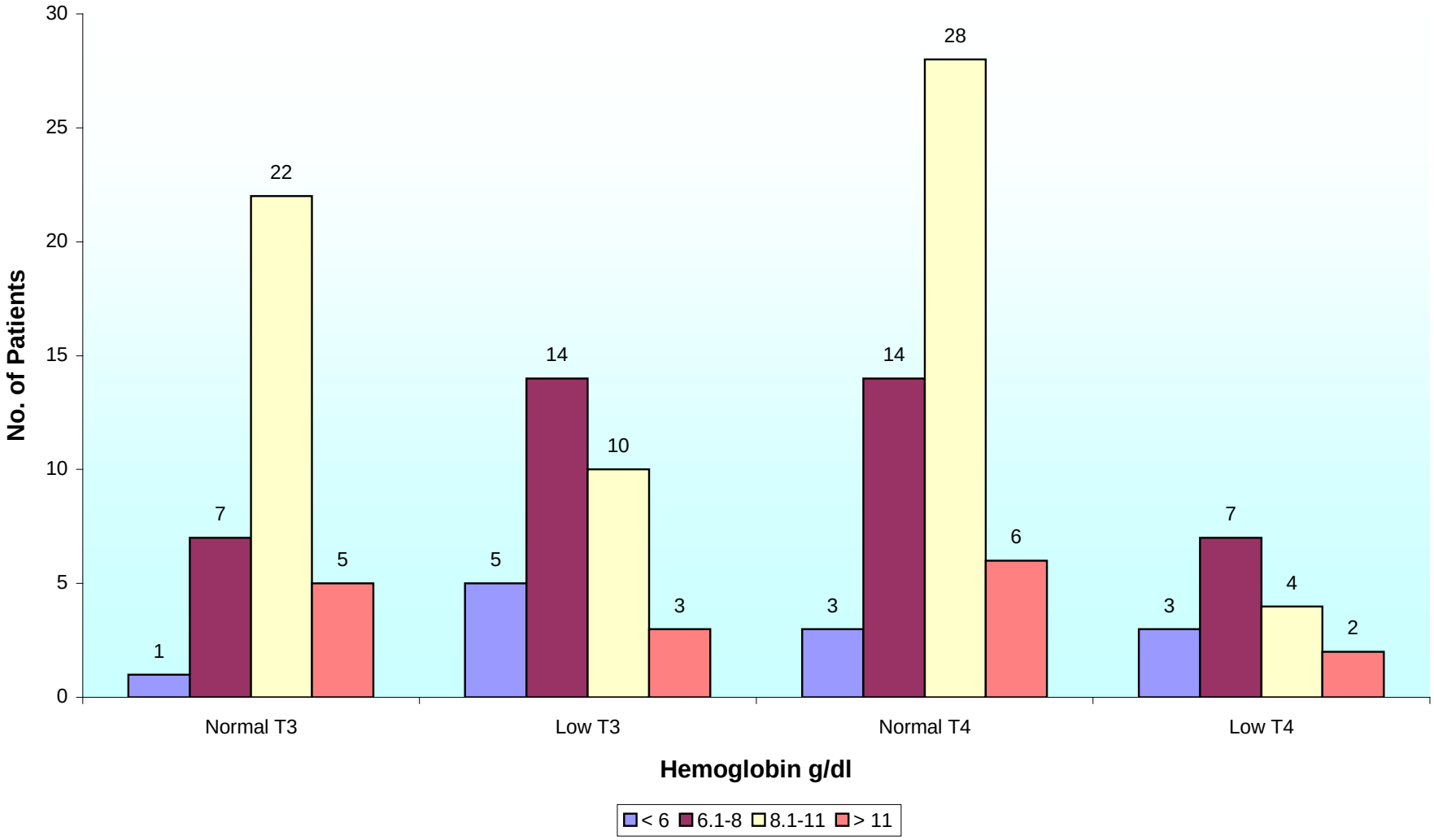


Figure - 8

Distribution of Serum T3 and T4 with Hemoglobin Levels



Discussion

DISCUSSION

Thyroid dysfunction in chronic kidney disease was studied by various authors. All the studies conducted till now do not reveal consistent results.

Thyroid dysfunction in CKD was extensively studied by Ramirez et al.[Ref.34,35] He studied thyroid abnormalities and he extensively researched about hypophyseal abnormalities in uremia. He compared CKD patients on conservative management and hemodialysis. His studies revealed low T3 and T4 levels. TSH was within normal limits. His study showed linear correlation between the mean T3 andT4 and severity of renal failure. TSH does not show any linear correlation with severity of renal failure.

Avasthi G et al., from Ludhiana studied thyroid function in patients of chronic kidney diseases.[Ref.1] Mean serum T3 and T4 values were significantly deceased in his study. This study revealed high serum TSH levels suggesting maintenance of pituitary thyroid axis. This result is comparable with Joseph et al., study.[Ref. 29] In contrast, Spector et al.,[Ref.41] and Ramirez et al.,[Ref.34] reported normal levels of serum TSH in patients of CKD in spite of low serum T3 levels. They demonstrated

abnormality in the hypophyseal mechanism of TSH release in uremia patients as the TSH response to the administration of thyrotropin releasing hormone (TRH) was blunted.

PD Rath and PK Padhi from Cuttack did a study on thyroid function status in chronic kidney disease on conservative management.[Ref. 32] They concluded both serum T3 and T4 were deceased, TSH was not significantly increased.

Joseph LJ, Mehta HJ from Bombay conducted a study on total and free thyroid hormone levels in CKD.[Ref.29] They had taken thyroid profile in 127 CKD patients. Their results showed decreased T3 and T4 with no significant change in TSH value. This study's results are consistent with the results of Xess A and Gupta A from Patna's study on evaluation of thyroid hormones in CKD.[Ref.47] They analysed 62 patients on conservative management and 34 patients on chronic hemodialysis. They also concluded that chronic hemodialysis did not have a positive effect in alteration of serum T3, T4 and TSH levels.

Spector DA et al., studied 38 patients with CKD for thyroid function and metabolic state.[Ref.41] Mean values for serum T4 and T3

were within normal limits. But 43% of the patients had low serum T3. Serum TSH concentrations were normal.

Kayimo JE et al., from Nairobi, Kenya conducted a study in 52 patients with CKD.[Ref.26] This study results showed T3 and T4 were low and TSH levels were significantly higher.

Kaptien EM et al., from Los Angles, USA studied thyroid hormone metabolism and thyroid disease in CKD.[Ref.23] In his study, serum T3 and T4 are reduced, with blunted TSH response to TRH. He concluded dialysis therapy minimally affects thyroid hormone metabolism and thyroid hormone metabolism normalises with renal transplantation.

In our study patients only on conservative management were studied. This is because thyroid profile undergoes changes due to dialysis.

In our study 53.3% of the patients have thyroid profile abnormalities. Remaining 46.7% of patients had normal thyroid profile. Among the patients with thyroid dysfunction hypothyroidism is present in 10.7% of patients. Excluding the primary hypothyroidism patients 42.7% of patients have decreased serum T3 values (low T3 syndrome).

Among these low T3 syndrome patients 21.3% of patients also have decreased serum T4 value (low T4 syndrome). The percentage of patient who have low T3 syndrome increases with the decrease in creatinine clearance, which is statistically significant. The increase of low T4 percentage does not show this linear relationship with creantinine clearance.

Many studies conducted in CKD patients showed low T3 values.[Ref. 1,2,17,27,34,39,41] Low T4 had been reported in Ramirez et al., Hegedus et al., Backett et al., studies.

In our study the mean T3 value is below normal limit. After Excluding hypothyroidism patients the mean T3 value is within low normal limits. Mean T3 value progressively decreases with decline in creatinine clearance. This mean T3 value has a linear correlation with severity of renal disease which is statistically significant. This linear correlation between mean T3 and severity of renal failure is consistent with the studies of Ramirez et al., and Spector et al.

The mean T4 level in our study is below normal in creatinine clearance less than 10 ml/min group. In all other levels of creatinine clearance the mean T4 value is in low normal level and T4 does not correlate with the severity of renal failure. This is consistent with Avasthi et al., study.

Excluding hypothyroidism mean TSH level in our study is within normal limits. The mean TSH levels are also within normal limits for the various ranges of creatinine clearance. The TSH level does not show any linear correlation with the severity of renal failure. This is consistent with the studies of Spector et al. and Ramirez et al.

In our study excluding those with hypothyroidism, 14 patients have slightly elevated TSH. Eight patients had TSH in the range of 10 to 20 µIU/ml. In these eight patients only five have low T4 levels, among them only one patient had few clinical features of hypothyroidism. Investigation like free T4, Free T3, TRM response and antithyroid antibodies can be done to diagnose hypothyroidism in these patients.

In our study anemia was almost universal in CKD patients. The degree of anemia had a linear correlation with both mean T3 and mean T4 values which were statistically significant.

Our study was consistent with the results of Ramirez et al., study showing low T3, low T4 and normal TSH. From the various studies it has been suggested that these thyroid profile derangements are part of the body adaptation mechanism.

Dialysis

Hemodialysis and continuous ambulatory peritoneal dialysis have shown to affect the thyroid profile independently of CKD. Also drugs like heparin, frusemide used during dialysis will affect the thyroid profile.

Kayima et al., and Giardana et al., have conducted studies on the effect of dialysis on CKD patients with thyroid dysfunction. These studies showed no significant improvement in thyroid profile after repeated hemodialysis.

But in patients who had undergone renal transplant surgery. Most of the thyroid function parameters returned to normal with TSH below normal.[Ref. 4,42]

Hypothyroidism

Previous studies conducted in patients with CKD, reported increased prevalence of hypothyroidism. Quion Verde et al., reported about 5% prevalence with terminal renal failure.[Ref.33]

Study by Kaptien et al., estimated the prevalence of primary hypothyroidism in CKD was about 2.5 times more frequent. The hyperthyroidism in CKD was estimated to range between 0 and 9.5%

Kaptein study also estimated the presence of antithyroid antibody in 6.7% of CKD patients.

In our study hypothyroidism was present in 10.67% of patients. The prevalence of hypothyroidism does not correlate with the severity of renal failure. The symptoms of hypothyroidism are present both in CKD with hypothyroidism patients and in CKD patients without hypothyroidism.

So diagnosis of hypothyroidism in CKD mainly relies on TSH level which should be more than 20 µIU/ml with low serum T4.

In this study no patient had clinical or biochemical features of hyperthyroidism.

Goitre

Remirez et al., reported high prevalence of goitre in CKD. The incidence of goitre has also been variably reported in various studies.[Ref.1,28,34,41,48] The possible explanations for the increased incidence is due to accumulations of iodides in thyroid gland due to decreased renal clearance in CKD patients. Apart from goitre study

conducted by Hegedus et al., showed thyroid gland volume was significantly increased in patients with CKD.[Ref.17)]

In our study only 3 patients had goitre but without clinical or biochemical features of hypothyroidism. Two of the patients had normal serum T3 and T4. One patient had low T3 and T4 with normal TSH . The number of patients with goitre in our study was statistically insignificant.

Conclusions

CONCLUSIONS

1. Thyroid dysfunction occurs both clinically and biochemically in CKD.

2. Thyroid dysfunction occurs in 53.3% of chronic kidney disease patients.

3. Incidence of hypothyroidism is 10.7% in CKD patients which is higher than that of general population.

4. Both clinical and biochemical parameters are essential to diagnose hypothyroidism in patients with CKD.

5. Excluding patients with hypothyroidism serum T3 level is low (Low T3 Syndrome) in 42.7% of patients and serum T4 is low (Low T4 Syndrome) in21.3% of patients with CKD.

6. Number of patients with low T3 progressively increases with severity of renal failure.

7. Means Serum T3 level has a linear correlation with the severity of renal disease.

8. Number of patients having low T4 and mean serum T4 level does not correlate with severity of renal failure.

9. Blood Hemoglobin level has a linear correlation with severity of renal failure.

10. Alteration in the values of T3 and T4 are a part of body adaptation mechanism to conserve energy.

11. Serum TSH level is normal in all stages of CKD excluding primary hypothyroidism.

Summary

SUMMARY

Patients with chronic kidney diseases have many symptoms and signs suggestive of thyroid dysfunction. It is very difficult to exclude the diagnosis of hypothyroidism on clinical grounds. So a study was conducted in CKD patients to study the prevalence and types of thyroid dysfunction and the correlation between thyroid dysfunction and severity of renal insufficiency if any.

Seventy five CKD patients on conservative management admitted in Institute of Internal Medicine Madras Medical College and Government General Hospital, Chennai were studied after taking consent. A detailed history and clinical examination were done. Investigations including serum T3, T4, TSH were done.

Eight patients had low serum T3, T4 and high TSH value of more than 20 µIU/ml. These patients were grouped under *"Primary hypothyroidism"*. Hypothyroidism incidence in CKD in this study is 10.67%. Low T3 syndrome incidence was 42.67%. No thyroid dysfunction occurs in 46.67% of CKD patients. Low T3 syndrome and mean serum T3 level had a linear correlation with severity of renal failure which was statistically significant.

Number of patients with low T4 was 21.33% after excluding hypothyroidism patients. The incidence of low T4 and mean serum T4 level does not correlate with severity of renal insufficiency. The mean value of serum TSH is within normal limits in all stages of renal failure excluding hypothyroidism.

Anemia was almost always present in CKD patients. As the hemoglobin decreases the incidence of low T3 syndrome increased. The mean serum T3 and T4 had a linear correlation with hemoglobin level which was statistically significant. To conclude thyroid dysfunction occurs both clinically and biochemically in patients with CKD. Both clinical and biochemical parameters are essential to diagnose hypothyroidism in these patients.

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LIST OF TABLES

LIST OF FIGURES

Proforma

PROFORMA

THYROID PROFILE IN CHRONIC KIDNEY DISEASE

NAME **AGE / SEX**

IP NO. **WEIGHT**

HEIGHT

COMPLAINTS **DURATION**

Breathlessness

Pedal Edema

Oliguria

Fatigue, weakness

Cold intolerance

Hoarse voice

Dry Sin

Weight Gain

Constipation

Sleep Disturbance

Others

PAST HISTORY

Hypertension	:	Y / N
Diabetes Mellitus	:	Y / N
Drugs	:	Y / N
Jaundice	:	Y / N
Trauma / Recent Surgery	:	Y / N
Other Systemic Illness	:	Y / N

MENSTRUAL AND OBSTETRIC HISTORY

GENERAL EXAMINATION

Nourishment	PR
Pallor	BP
Facial Puffiness	BP

Pedal Edema

Skin Texture RR

Thyroid Swelling

TEMP

CVS

RS

Abdomen

CNS

INVESTIGATION

Hb gm/dl

TC Cells / cumm

DC P % L % E %

ESR

Peripheral Smear

Urea : mg/dl

Creatinine : mg/dl

Sugar : mg/dl

Na^{+} : MEq/L

K^{+} : Meq/L

Ca^{++} : mg/dl

Po_4^{3-} : mg/dl

URINE EXAMINATION

Albumin

Sugar

Deposits

LIVER FUNCTIONS TESTS

T. Protein : g/dl

Albumin : g/dl

Globulin : g/dl

Serum Lipid Profile

Cholesterol : mg/dl

Creatinine Clearance : ml/min

12 Lead ECG

CHEST X RAY

USG ABDOMEN

Thyroid Profile

T3 : ng/ml

T4 : µg/dl

TSH : µIU/ml

Master Chart

MASTER CHART

Sl. No.	Name	Age	Sex	I.P.No.	Symptoms Duration	Hemoglobin g/dl	Renal parameters			Ultrasound abdomen	Thyroid Profile			Miscell-aneous
							Urea mg/dl	Creatinine mg/dl	Creatinine clearance ml/min		T3 ng/ml	T4 µg/ml	TGH µlU/ml	
	Rajamanickam	40	M	782575	24 months	6.8	138	8.2	9	1	0.5	7.4	0.8	1
	Shanawaz	20	M	784263	8 months	9.6	116	4.8	17	1	0.7	5.8	2.0	1
	Lakshmi	58	F	797437	6 months	10.8	65	2.4	18	1	0.3	7.2	1.9	
	Kesavan	56	M	799818	12 months	9.2	88	4.2	13	1	1.9	6.7	0.8	1
	Periyadurai	50	M	800875	6 months	10.6	79	2.8	22	1	1.1	6.1	2.1	
	Kettyvel	70	M	801409	24 months	11.2	82	2.3	20	1	0.5	3.1	1.4	1
	Jayabalan	28	M	801306	18 months	12.1	90	2.6	38	1	1.9	6.7	5.2	
	Sigamani	52	M	800069	5 months	8.4	105	4.5	14	2	0.2	2.1	28.5	1
	Samudeen	55	M	801707	4 months	7.8	112	5.8	10	1	0.3	6.7	2.1	1
	Varghees	76	M	801756	12 months	9.1	92	2.8	16	1	0.7	7.1	3.1	1, 2
	Natarajan	52	M	799584	4 months	8.2	73	2.4	21	1	1.9	6.9	2.9	2
	Ramamoorthy	35	M	800363	24 months	6.4	124	6.3	13	1	0.3	6.2	12.7	1
	Panneerselvam	38	M	800399	12 months	10.8	78	4.6	34	1	0.7	9.2	2.7	

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							Urea mg/dl	Creatinine mg/dl	Creatinine clearance ml/min		T3 ng/ml	T4 µg/ml	TGH µlU/ml	
	Munusamy	52	M	803620	6 months	11.4	81	3.6	22	1	0.8	8.3	1.0	1
	Ettayan	57	M	802627	8 months	11.8	67	2.7	24	1	0.5	3.7	1.3	
	Nagarajan	50	M	805401	24 months	7.8	68	3.4	14	1	0.3	1.1	25	1
	Muthaiyan	62	M	805194	18 months	7.9	76	4.2	13	1	0.7	5.7	1.9	1
	Sangeetha	20	F	807931	6 months	10.8	68	3.1	25	1	0.5	3.6	12.5	1
	Panneerselvam	43	M	809013	8 months	7.2	98	5.0	11	1	0.2	7.9	1.2	
	Velu	60	M	804894	4 months	10.8	78	2.6	20	2	0.7	8.9	3.4	2
	Gopal	60	M	804823	12 months	4.8	125	6.1	8	1	0.4	2.6	1.2	1
	Egambaram	72	M	810895	4 months	5.2	102	4.2	10	1	0.8	7.9	1.9	1
	Seetharaman	67	M	810880	30 months	11.1	87	2.8	24	1	0.4	2.6	24.0	1, 2
	Saraswathy	55	F	809858	4 months	10.2	110	2.4	28	1	1.2	7.2	6.2	4
	Pattabiram	54	M	811343	12 months	6.9	88	3.6	18	1	0.3	7.4	2.9	1
	Ponnamma	58	F	817081	36 months	5.1	110	5.2	10	2	0.4	6.4	11.6	1
	Anbu	30	M	810181	24 months	8.9	88	4.8	20	1	1.7	7.1	0.8	

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							Urea mg/dl	Creatinine mg/dl	Creatinine clearance ml/min		T3 ng/ml	T4 µg/ml	TGH µlU/ml	
	Munivel	60	M	812877	8 months	7.0	84	5.0	12	1	0.5	3.2	2.3	1
	Kalaiselvan	30	M	815110	8 months	10.4	79	3.1	31		2.0	7.3	2.1	1
	Durai	38	M	815053	12 months	9.8	107	4.6	18	1	0.2	7.9	3.6	
	Natesan	48	M	811860	18 months	6.2	124	8.2	10	1	0.3	3.2	3.1	1
	Rajalingam	52	M	818276	4 months	8.2	84	2.2	36	1	1.0	8.1	1.1	1
	Rangasamy	47	M	817952	6 months	7.8	95	6.1	12	1	0.5	3.6	14.5	3
	krishnan	65	M	818859	4 months	9.8	78	3.0	20	1	0.4	9.6	3.7	2
	Pushpavathy	48	F	819941	8 months	11.8	146	4.4	12	1	0.4	4.1	26.0	1
	Chellamma	36	F	821874	6 months	12.4	78	2.2	38	1	1.7	8.9	5.6	
	Usena	45	F	823487	8 months	8.2	92	3.6	16	1	0.5	4.1	3.2	1
	Thangavel	65	M	820352	4 months	7.6	68	3.0	18	1	0.7	6.1	0.5	1
	Ponnudurai	55	M	823695	6 months	9.8	79	2.6	31	1	0.8	6.7	3.5	1
	Ashokan	40	M	824023	3 months	7.6	124	7.6	10	2	0.5	2.4	25.0	1, 2
	Purushothaman	54	M	821183	4 months	9.8	112	4.9	13	1	0.8	9.1	1.9	4

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							Urea mg/dl	Creatinine mg/dl	Creatinine clearance ml/min		T3 ng/ml	T4 µg/ml	TGH µlU/ml	
	Periyasamy	50	M	828518	6 months	10.2	87	3.5	18	2	0.3	8.2	10.5	1
	Velmurugan	22	M	824531	8 months	4.2	163	13.6	8	1	0.2	1.7	7.6	3
	Saravanan	35	M	825135	12 months	6.4	185	10.4	8	1	0.3	6.1	1.8	1
	Raja	26	M	824239	6 months	6.9	96	4.6	18	1	0.7	5.5	0.7	1
	Palani	40	M	824324	4 months	10.4	82	2.8	31	1	1.1	7.9	2.3	1
	Narayanasami	55	M	825916	3 months	7.9	82	3.4	14	2	0.5	4.1	1.7	
	Gunasekaran	41	M	825977	15 months	8.4	82	3.3	24	1	0.4	1.5	27.0	1
	Chinnaiya	62	M	824689	6 months	8.2	78	3.1	20	1	0.7	5.8	1.3	
	Parthasarathy	65	M	826661	6 months	6.9	83	3.4	12	1	1.0	7.0	0.8	1
	Boopathy	42	M	825156	8 months	11.4	72	2.8	36	1	0.5	7.0	14.0	2
	Krishnan	57	M	827184	4 months	7.4	71	2.8	18	1	0.2	3.1	1.4	1
	Rajinath	55	F	826637	24 months	6.9	92	4.2	12	1	1.3	6.1	1.2	1
	Suryakandha	65	F	826822	6 months	8.2	80	2.8	20	1	0.9	7.1	1.4	1
	Arputham	28	F	826264	6 months	10.4	72	2.7	18	2	0.3	0.8	26.5	1

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	Periyasamy	53	M	828228	8 months	10.2	77	3.4	17	1	0.7	6.4	1.0	
	Sami	58	M	828560	4 months	9.6	68	2.4	22	1	0.9	6.1	0.7	
	Govindasami	44	M	829444	3 months	11.2	74	2.6	34	1	0.7	6.2	2.1	1
	Murugan	35	M	828026	24 months	4.7	170	14.7	7	1	0.2	2.2	13.5	3
	Vincent	50	M	832631	6 months	8.2	82	3.2	16	1	0.4	8.9	2.1	2
	Sekar	37	M	833794	9 months	9.4	96	4.2	13	1	0.2	3.2	6.3	
	Munaram	30	M	833619	12 months	7.2	81	6.4	11	1	0.4	2.1	3.1	1
	Arundoss	20	M	832247	4 months	10.4	74	3.2	36	1	0.9	7.1	2.4	1
	Ajesh	42	M	832237	6 months	9.8	96	3.2	24	2	0.5	3.9	3.1	
	Sundaralingam	47	M	838135	12 months	7.2	115	5.1	10	1	1.1	7.9	2.1	1
	Stellamary	24	F	833480	12 months	5.2	154	8.2	8	1	0.2	6.1	1.3	1
	Mannarammal	65	F	834372	4 months	7.8	82	2.6	13	1	0.4	3.1	1.1	4
	Chakkamma	50	F	832367	6 months	9.2	84	3.1	17	1	1.2	5.7	1.3	1
	Duraisamiammal	56	F	831248	8 months	8.2	160	4.2	10	2	0.7	5.8	0.7	1, 2

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	Pataiyan	55	M	808971	6 months	7.9	98	5.1	12	1	0.8	6.3	1.7	
	Rahman Sheriff	54	M	831585	24 months	8.2	122	5.7	10	1	0.3	3.2	24.5	1
	Lakshmi Kandha	38	F	834889	3 months	10.2	76	2.4	35	1	0.5	7.2	5.1	2
	Padrattan	66	M	837204	3 months	7.8	82	2.3	18	1	0.4	5.5	13.5	2
	Suresh Babu	40	M	836500	6 months	8.9	90	2.5	34	2	0.8	6.2	1.5	
	Shankar	42	M	836778	12 months	12.2	102	3.1	28	1	0.9	6.9	0.9	1

ULTRASOUND ABDOMEN

1 - Bilaterally Contracted Kidneys

2 - Corticomedullary Differentiation Lost

MISCELLANEOUS

1 - Hyptothyroid symptoms present

2 - Delayed Ankle Jerk

3 - Papilledema present

4 - Goitre Present